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AMINO ACIDS AND THEIR DERIVATIVES IN BLOOD PLASMA OF PATIENTS WITH BREAST CANCER TREATED WITH UKRAIN. PART V

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Summary: *The present study was undertaken to evaluate the influence of Ukrain on the free amino acids pool in blood plasma in ten patients with breast cancer, treated in the preoperative phase with the drug. The control group consisted of five patients of similar age and advancement of the disease, who did not receive Ukrain before mastectomy. The data obtained from these studies indicate that Ukrain positively influences the metabolism of amino acids and their derivatives. The most characteristic changes were increase of proline, taurine and glutamic acid.*

Introduction

It has recently been found that patients with malignancies may develop both intra- and extracellular disturbances in the amino acid (AA) pool metabolism (1, 2). This phenomenon may be explained in part by different AA metabolism of malignant tissue which uses for its growth more of a host endogenous AA pool (3). In consequence a negative nitrogen balance may be observed (1). The rising AA pool imbalance may be responsible for anorexia and starvation observed in patients with malignancies (4, 5).

Recent methods used for treatment of malignant diseases do not alleviate the AA pool metabolism of the patient but may even aggravate it (6-8). Some information indicates that a relative normalization of the AA pool in a patient with malignancy may positively influence the efficacy of antitumour therapy and may improve the clinical status of the patient (7, 8).

Patients and methods

Ten women with stage T1-3N0-1M0 breast cancer were selected for the study. Before radical mastectomy each patient was treated with Ukrain. The drug was injected 10 times, intravenously, every second day in a dose of 5 mg Ukrain. Surgery was performed 7-10 days after discontinuation of treatment. For analysis of the AA pool

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and their derivatives (AADs) blood was taken from a vein before and after treatment with the drug.

Free AA and AADs were determined in perchloric acid extracts from blood plasma in a T-339M amino acid analyser, using the method of Benson (9) with Nefyodov's and colleagues' modification. The results obtained were processed in the multichrome programme complex.

The multivariant analysis (correlation, discriminant) and data processing were prepared using the 3d and 7m computer programmes from the BMDPC package (10, 11).

Results

As presented in Table I, the concentrations of AAs as well as other compounds studied considerably exceeded those observed in healthy blood donors in the blood plasma of patients with breast cancer, with the exceptions of taurine, glutamic acid and proline. Application of Ukrain essentially did not affect the concentration of the majority of AAs and AADs. However, Ukrain induced enrichment of the total pool of free thiol-containing AAs, mostly taurine, increased the level of glutamic acid and proline and considerably decreased the level of alanine.

Table I Concentration of free amino acids and their derivatives in tumour tissue of patients with breast cancer treated with Ukrain

Compound	Concentration, μM	
	On admission (n=10)	After Ukrain treatment (n=10)
Cysteic acid	10.9±1.1	11.3±0.8
Taurine	102.5±6.0	140.2±7.74*
Urea	321.6±33.5	361.0±31.4
Aspartic acid	33.0±9.0	59.1±28.7
Threonine	137.1±12.4	131.7±8.8
Serine	163.0±12.5	156.9±4.6
Asparagine	43.5±3.7	42.0±6.4
Glutamic acid	56.7±13.1	52.1±10.9
Glutamine	420.6±44.3	644.1±52.4*
Proline	126.3±9.5	246.1±23.1*
Glycine	342.3±36.1	290.0±26.7
Alanine	500.6±20.5	394.6±27.6*
α-aminobutyrate	24.1±1.9	25.1±2.8
Valine	216.9±14.1	224.2±17.0
Cystine	94.0±9.1	91.3±7.5
Methionine	26.6±2.2	25.5±0.8
Cystathionine	3.5±0.9	4.8±0.8
Isoleucine	62.7±5.2	62.2±6.5
Leucine	130.7±10.1	124.8±10.8
Tyrosine	73.8±5.8	69.9±3.4
Phenylalanine	58.6±4.1	58.6±2.2
β-alanine	3.6±1.8	2.1±0.7
Ethanolamine	45.9±3.2	40.9±5.1
Ammonia	206.2±74.4	284.4±36.1
Ornithine	115.1±12.2	119.6±8.9
Lysine	22.3±17.7	19.6±7.8
Histidine	80.6±5.6	75.4±4.0

* $p < 0.05$

Discussion

As presented under Results, the concentration of the majority of the compounds analysed exceeded those observed in the plasma of healthy blood donors from the Transfusion Station in Grodno (12). In general these data are in agreement with the literature reporting hyperaminoacidaemia in patients with malignant tumours (7, 13, 14). An exception was the decrease in the levels of taurine, glutamic acid and proline at an average of 25 percent as compared with healthy individuals (12) or with patients with no tumour disease of the hepatobiliary tract admitted to the Surgical Department of the Grodno Medical Centre (15). The decreased concentration of plasma-free taurine found in our patients can be explained by the disturbed catabolism of thiol-containing AAs and their enhanced excretion in urine (15), whereas the eliminated content of glutamic acid and the product of its conversion, proline, may be interpreted as a result of inhibition of glutamine dehydrogenase activity and biosynthetic processes of the whole AA pool (16).

Application of Ukrain essentially did not change the concentration of the majority of the AAs and AADs, except for the increase of taurine, glutamic acid and proline (Table I). Taking into account that taurine is a highly biologically active molecule with antioxidative and radioprotective potential, its increase due to Ukrain treatment is beneficially adaptogenic to the body from the metabolic viewpoint. An additional positive effect of

Ukrain on the formation of a plasma-free AA pool is the relative increase in the concentration of glutamic acid which, with the concentration of alanine diminished in parallel, confirmed by inhibition of Alat, may indirectly indicate the improvement of the liver detoxifying function (6). These observations are supported by data of the linear-discriminant analysis, with the most informative parameters being alanine, taurine, cystathionine, cystine and glutamic acid. All were changed after Ukrain administration and the values for the Fisher constant decreased from 17 to 7 (17).

The twofold increase in the concentration of free proline in the plasma of patients treated with Ukrain is worth special attention (Table I). Hydrolysis of the endogenous protein and proline-containing polypeptides of the tumour tissue, due to the cytolytic properties of Ukrain, may explain this phenomenon. This point of view seems to be supported by data indicating an increased proline content in the tumour tissue of patients treated with Ukrain (6) as well as by both histological and electronmicroscopic observations indicating an intensive proliferation of connective tissue in breast carcinomas of patients injected with the drug (4).

The above observations indicate that Ukrain, besides a local malignotoxic effect on breast cancer as well as on other malignancies (17-19), may positively influence the metabolism of AAs and AADs, contrary to other cytostatics and radiotherapy being metabolically destructive. This observation has important clinical value in the management of patients with malignancies, particularly those in an advanced stage of the disease.

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